

# **CORDBLOOD ACRYLAMIDE AND GLYCIDAMIDE HAEMOGLOBIN ADDUCTS, METABOLIC POLYMORPHISMS AND MICRONUCLEUS FREQUENCY**

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**Background and Aims:** Exposure to acrylamide (AA) in the non-smoking general population occurs almost exclusively via foods cooked at higher temperatures (i.e., potato chips and fries). AA is metabolized to glycidamide (GA by cytochrome P450 enzyme 2E1, CYP2E1). AA and GA bind to glutathione and are excreted with the urine. Concerns about acrylamide exposure in utero and the risk of adverse health effects are justified by AA/GA potential carcinogenicity. Hemoglobin adducts (HbAA and HbGA) are well-established biomarkers of exposure to these chemicals. The cytokinesis-block micronucleus assay (CBMN) quantifies early genetic effects associated with cancer risk. Furthermore, individuals may be at increased risk due to particular genetic predisposition. The relationship between cord blood HbAA and HbGA and the frequency of micronuclei in cord blood lymphocytes, and the effect of CYP2E1 (Rs2480258 and Rs915906 single nucleotide polymorphisms) were studied in EU funded Integrated Project NewGeneris (Newborns and Genotoxic exposure risks).

**Methods:** The study included newborns from Greece, Norway, Spain, Denmark, and the United Kingdom (n.=1040) whose mother gave informed consent at recruitment. Hb adducts were measured by the "adduct FIRE procedure" using LC-tandem mass spectrometry. CBMN assay was used to measure micronuclei in binucleated and mononucleated cells (n.= 470).

**Results:** HbAA and HbGA were highly correlated ( $r=0.85$ ,  $p<0.0001$ ). Multiple regression analysis failed to show a linear relationship between HbAA and the frequency of micronucleated-binucleated cells ( $p\text{-trend}=0.161$ ) but revealed an increased frequency of micronucleated-binucleated cells in the highest quintile of HbAA compared to the lowest quintile ( $RR= 1.36$ ,  $95\%CI: 1.00\text{-}1.86$ ,  $p=0.05$ ). The CYP2E1 variant was associated with a 50% higher frequency of micronuclei in binucleated cells ( $RR=1.53$ ,  $95\%CI:1.02\text{-}2.23$ ,  $p=0.04$ ).

**Conclusions:** The association between cord blood hemoglobin adducts from AA and micronuclei frequency is suggestive of the role of a maternal intake of foods with a high content of acrylamide during pregnancy and genotoxic effects on the fetus, with CYP2E1 enzyme possibly playing a role as an effect modifier.